68Gallium-DOTATATE PET in meningioma: A reliable predictor of tumor growth rate?

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Abstract: BACKGROUND DOTATATE-based radionuclides have added new options in the diagnosis and treatment of meningiomas; however, a reliable predictor of tumor growth has still not been established. METHODS We analyzed 64 meningiomas imaged with (68)Ga-DOTATATE PET. Tumor growth rates were calculated by volumetric analysis of sequential MRI scans. Maximums of standardized uptake values (SUVmax) were correlated with tumor growth and covariates. RESULTS World Health Organization (WHO) grades I and II meningiomas showed a correlation of SUVmax and tumor growth rate (meningiomas limited to the intracranial compartment: $r = 0.757$, $P < .001$, and transosseous growing meningiomas: $r = 0.819$, $P = .024$). SUVmax was significantly higher and the slope of the linear regression significantly steeper in transosseous compared with intracranial meningiomas (both $P < .001$). The association remained significant in multivariate analysis, and the prediction of tumor growth rate was independent of WHO grade. Anaplastic meningiomas showed no significant correlation of SUVmax and tumor growth. CONCLUSIONS (68)Ga-DOTATATE PET is a reliable predictor of tumor growth in WHO grades I and II meningiomas and provides additional information to conventional cross-sectional imaging modalities. Hence, (68)Ga-DOTATATE PET can assist in selecting the time point for treatment initiation. Furthermore, meningiomas with fast tumor growth and transosseous expansion elicit the highest DOTATATE binding; therefore, they might be especially suited for DOTATATE-based therapy.

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^{68}Gallium-DOTATATE PET in meningioma: A reliable predictor of tumor growth rate?

Running title: prediction of meningioma growth rate

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Abstract

Background: DOTATATE based radionuclides have added new options in the diagnosis and treatment of meningiomas; however, a reliable predictor of tumor growth has still not been established.

Methods: Analysis of 64 meningiomas imaged with ^{68}Ga-DOTATATE positron emission tomography (PET). Tumor growth rates were calculated by volumetric analysis of sequential MRI scans. Maximum of standardized uptake values (SUVmax) were correlated with tumor growth and co-variates.

Results: WHO grades I and II meningiomas showed a correlation of SUVmax and tumor growth rate (meningiomas limited to the intracranial compartment: $r=0.757$, $p<0.001$, and transosseous growing meningiomas: $r=0.819$, $p=0.024$). SUVmax was significantly higher and the slope of the linear regression significantly steeper in transosseous compared to intracranial meningiomas (both $p<0.001$). The association remained significant in multivariate analysis and the prediction of tumor growth rate was independent of WHO grade. Anaplastic meningiomas showed no significant correlation of SUVmax and tumor growth.

Conclusion: ^{68}Ga-DOTATATE PET is a reliable predictor of tumor growth in WHO grades I and II meningiomas and provides additional information to conventional cross-sectional imaging modalities. Hence, ^{68}Ga-DOTATATE PET can assist in selecting the time point for treatment initiation. Furthermore, meningiomas with fast tumor growth and transosseous expansion elicit the highest DOTATATE binding; therefore, they might be especially suited for DOTATATE- based therapy.

Key words: DOTATATE-PET; DOTATOC-PET; Meningioma; SSTR2

Introduction

Meningiomas, with an annual incidence of 2.3 per 100,000, are the most common primary central nervous system (CNS) tumors and comprise nearly 34% of all CNS tumors.[1-3] According to the World Health Organization (WHO), approximately 94% of meningiomas are classified as benign (WHO grade I), 5-7 % as atypical (WHO grade II) and 1-3% as anaplastic (WHO grade III).[4-7] WHO grade I tumors have a good prognosis with a recurrence rate of approximately 5% after 5 years following gross total resection. WHO grade II and III meningiomas, however, remain challenging to treat and show 5 year overall recurrence rates of approximately 40% and 80%, respectively.[1,2] Multiple simultaneous meningiomas are recognized, especially in the context of neurofibromatosis II, and usually display a uniform histology.[8,9]

The cross-sectional imaging modalities computed tomography (CT) and magnetic resonance imaging (MRI) are commonly applied for the identification and assessment of meningiomas.[10] In meningioma management, the assessment of tumor growth rate (TGR) is critical to select an appropriate time point for therapy initiation and type of treatment, with surgery as the mainstay of primary treatment. However, surgery is challenging in meningiomas located in the skull base region, due to frequent transosseous growth and the close relationship to cranial nerves and other delicate anatomical structures.[11]

Positron emission tomography (PET) with specific radiotracers is an imaging modality that adds molecular information. As meningiomas generally express somatostatin receptor subtype 2 (SSTR2),[12] octreotide based radiotracers with high affinity to these receptors are suitable tumor imaging tracers.[13] Primarily, ^{68}Gallium (Ga) labeled DOTATATE and DOTATOC tracers are used to determine the extent of SSTR2-

positive meningiomas.[14-18] Using ^{68}Ga-DOTATOC, Afshar-Oromieh and colleagues showed that PET has superior sensitivity in meningioma detection. Rachinger et al. demonstrated better tumor to non-tumor discrimination of PET/CT over contrast-enhanced MRI.[17-19] Furthermore, ^{68}Ga-DOTATOC PET/CT information may strongly complement MRI and CT for intensity-modulated radiation therapy (IMRT) planning in patients with complex meningiomas of the skull base region for intensity-modulated radiation therapy (IMRT) planning.[20]

In recent years, initial studies described ^{90}Y or ^{177}Lu radio-labeled somatostatin analogs to treat SSTR2-positive meningiomas. Bartolomei and colleagues demonstrated disease stabilization in 66% of patients with meningiomas after peptide receptor radionuclide therapy (PRRT),[21] which was confirmed in a recent study that reported a high percentage of patients with disease stabilization.[22] Accordingly, binding of the therapeutic radionuclide correlates with the pretherapeutic standardized uptake value (SUV) in PET, and ultimately with the SSTR2 expression of meningiomas.[18,23] However, these results are conflicting, since SSTR2 expression itself is supposed to lead to growth inhibition in neoplastic and non-neoplastic tissue.[24,25] Alternatively, binding may only reflect a more benign tumor behavior rather than beneficial response to therapy.

We aimed to study the SUV reflecting SSTR2 expression as measured by ^{68}Ga-DOTATATE PET and its correlation to tumor growth in subsequent MR scanning. We hypothesized that SSTR2 uptake in ^{68}Ga-DOTATATE PET not only accurately delineates meningiomas as previously reported but also provides critical information on tumor behavior for further treatment planning.

Materials and Methods

Patient population

All patients who received a ^{68}Ga-DOTATATE PET for meningioma imaging from 01/2011 to 12/2014 (n=45) were included in this study. Twenty-two patients were excluded because of insufficient MRI follow-up data, cerebral radiation therapy within the last two years or incomplete histological work-up. In patients with multiple meningiomas, we assessed up to a maximum of five separate lesions and analyzed the tumors with highest volume, resulting in 64 meningiomas from 23 patients. The study was approved by the local ethics committee (KEK-ZH 2014-0605).

PET and MR data acquisition

PET imaging was performed on a full ring PET/CT system (Discovery VCT, GE Healthcare, Waukesha, WI, United States of America). For attenuation correction purposes, a low-dose CT scan of the head was initially performed (10 mA, 120 kV, pitch of 0.984:1, collimation of 64 ×0.625 mm). The PET scan was initiated directly after the injection of 150 MBq ^{68}Ga-DOTATATE and emission data were acquired over 60 minutes (axial FOV of 153 mm covering the entire brain with one bed position). Emission data were corrected for randoms, dead time, scatter and attenuation and iteratively reconstructed (3 iterations, 18 subsets) using the CT.

We selected one brain MRI examination before ^{68}Ga-DOTATATE PET and another afterwards, resulting in at least 4 months of temporal difference between both images (median 11, minimum 4, maximum 20 months). All MRI examinations included axial T1- and T2-weighted images, and axial, coronal and sagittal T1 weighted images after the injection of Gadolinium contrast media (T1Gd).

PET and MR image analysis

A board-certified nuclear medicine physician analyzed the PET images using PMOD Version 3.4 (PMOD Technologies Ltd, Zurich, Switzerland) and measured the maximal SUV (SUVmax) value in all meningiomas. For the quantitative evaluation of the PET data, frames acquired between 40 and 60 minutes were averaged. In the PET data set, volumes of interest (VOIs) were adjusted in 3 planes so that the entire meningioma was included.

A second independent reader, blinded to the SUV, determined TGR of meningiomas in each patient. Meningiomas 'en plaque' were not assessed, as they are prone to measurement inaccuracies. As all other intracranial meningiomas corresponded approximately to a rotational ellipsoid, volume was calculated by multiplying the product of the three diameters by 0,523 (according to the formula $4/3*\pi*a*b*c$, whereas a, b, c are the lengths of each radius). The volumes of all transosseous meningiomas were determined by three-dimensional volumetric measurements (contour outline on all axial slices) on T1Gd images. Finally, the monthly growth rate was calculated by dividing the percentage change in size by the numbers of months between the two examinations.

Grading and histological assessment

Histological grading according to the WHO classification was performed in at least one of the meningiomas by a board-certified neuropathologist blinded to clinical and radiographic details.[4] Median time interval between histology and PET imaging was 5.9 months. Since the majority of simultaneously occurring multiple meningiomas show

a uniform histology,[8,9] all meningiomas from a given patient, even those that were not surgically sampled, were assigned the same WHO grade. To assess for potential bias when analyzing multiple meningiomas per patients, an additional evaluation with only one biopsied meningioma per patient was performed. For this additional assessment, we selected the largest meningioma, when histology of multiple meningiomas was available.

Concomitant therapy

We assessed concomitant therapy during MR follow-up and 5 patients received focal therapy (all WHO grade I or II), including stereotactic radiation (protons or photons) and embolization (total of 6/57 meningiomas), one patient with WHO grade III meningioma received systemic therapy with interferon alpha 2a. As all treatments aimed at tumor volume reduction or growth inhibition, we pooled treatments in statistical analysis.

Statistical analysis

Statistical analyses were performed using SPSS (version 21, IBM Corporation, Armonk, NY, USA). We calculated Pearson's r and linear regression analysis, with values of R^2 below 0.4 were considered weak, between 0.4 and 0.6 moderate and above 0.6 strong. We calculated significance of differences in regression slopes using the Chow test. In multivariate linear regression, SUVmax, age, sex, WHO grade, time between histology and PET, duration of follow-up, initial volume and concomitant therapy during follow-up were set as independent variables, and TGR as the dependent variable. Differences in mean values were tested with the Student's t-test. Significance was defined as $p<0.05$.

Results

Sixty-four meningiomas in 23 consecutive patients were analyzed (29 WHO grade I, 28 grade II and 7 grade III). TGR in relation to SUVmax of ^{68}Ga-DOTATATE PET is summarized in figure 1. Meningiomas were separated into three different clusters: transosseous growth, intracranial meningiomas of WHO grade I and II, and meningiomas of WHO grade III which were analyzed separately. Examples of PET and MR imaging of meningiomas are shown in figure 2.

Eighteen patients with 50 meningiomas of WHO grade I and II had tumor growth limited to the intracranial compartment. TGR of these meningiomas strongly correlated with SUVmax of ^{68}Ga-DOTATATE PET ($r=0.757$, $p<0.001$) and SUVmax correlated weakly with initial tumor volume in intracranial meningiomas ($r=0.316$, $p=0.025$) (**Fig.1**). In the patient analysis of biopsied meningiomas, correlation did not change ($r=0.907$, $p<0.001$). Both TGR and SUVmax did not differ in meningiomas with concomitant therapy during follow-up (n=4) versus non-treated meningiomas (n=46) (TGR: 9.8 ± 6.4 vs. 9.8 ± 8.1, $p=0.998$ and SUVmax: 10.5 ± 3.4 vs. 11.2 ± 7.4, $p=0.728$). Correlation coefficient of TGR and SUVmax was stable when calculated for medicated meningiomas only but like because of low patient numbers, not to a significant degree ($r=0.770$, $p=0.23$). In multivariate linear regression, SUVmax remained a strong predictor for TGR ($\beta=0.863$, $p<0.001$; only co-variate: initial tumor volume $\beta=-0.335$, $p<0.001$; $R^2=0.7$). Patients with intracranial meningiomas are summarized in **table 1**.

Seven meningiomas from 5 patients showed transosseous growth into the skull base or temporal squama (all WHO grade I; 3 patients had meningiomas with transosseous growth as well as tumors limited to the intracranial compartment) (**table 2)**. SUVmax values of these meningiomas were remarkably higher with a mean SUVmax of

43.3g/ml (range 18 - 70.7g/ml) compared to a mean SUVmax of 11.2g/ml (range 2.6 – 32.0g/ml) for meningiomas without transosseous growth ($p<0.001$). Additionally, the slope of the linear regression coefficient was steeper in meningiomas with transosseous growth compared to meningiomas restricted to the intracranial compartment ($a=5.5$ and $a=0.70$, respectively, $p<0.001$). Again, TGR of transosseous meningiomas correlated significantly with SUVmax of ^{68}Ga-DOTATATE PET ($r=0.819$, $p=0.024$) (**Fig.1**). The correlation coefficient remained stable at a high level in per patient analysis of biopsied meningiomas; however, like because of low patient numbers, not to a significant degree ($r=0.789$, $p=0.113$). TGR and SUVmax were concordantly lower in transosseous meningiomas (n=2) with treatment during follow-up versus non medicated meningiomas (n=5) (TGR: 5.8 ± 4.4 vs. 7.6 ± 2.9, $p=0.667$ and SUVmax: 34.1 ± 2.7 vs. 45.5 ± 24.6, $p=0.361$). SUVmax did not correlate with initial tumor volume in these meningiomas ($p=0.251$) and it was the only predictor of TGR in multivariate linear regression analysis ($\beta=0.818$, $p=0.024$, $R^2=0.7$).

WHO grade III meningiomas showed no significant correlation between TGR and SUVmax ($p=0.518$) (**Fig.1**). The monthly growth was remarkably high with relatively low SUVmax values (**table 3)**.

Discussion

Our study provides convincing evidence that high expression of SSTR2 as measured by SUVmax in Ga^{68}-DOTATATE PET predicts faster growth in WHO grade I and II meningiomas whereas WHO grade III meningiomas did not show an association of TGR with tracer binding. Meningiomas with transosseous growth elicited considerably higher Ga^{68}-DOTATATE binding.

These data are surprising, since SSTR2 expression itself is supposed to lead to growth inhibition in various neoplastic tissues.[24,25] The (patho-) physiological relevance of SSTR2 overexpression in meningiomas is not well understood,[26] and growth stimulation in the presence of somatostation and its analogue octreotide has been reported.[27] The Inhibitory effect of somatostatin in meningiomas is further challenged by the disappointing results of current treatment trials using somatostatin analogues.[28,29]

The predictive value of TGR with Ga^{68}-DOTATATE PET may be especially informative in meningiomas adjacent to delicate structures such as cranial nerves or arteries. Spefically, TGR with Ga^{68}-DOTATATE PET may help in planning the optimal time point for surgery and for follow-up imaging. This is especially valuable for newly diagnosed meningiomas in such critical locations. SUVmax remains an independent predictor of TGR estimation in multivariate analysis, including tumor size and WHO grade, providing additional information to these estimates. Further studies have to assess the potential changes in management by the treating physician or the advisory tumor board in order to establish corresponding recommendations.

Our results also support further development of PRRT in meningiomas. As noted, Rachinger and colleagues showed a strong congruence of SUVmax in Ga^{68}-DOTATATE PET with SSTR2 expression in the histologic preparations.[18] In addition, Ga^{68}-

DOTATATE PET SUVmax correlates with radionuclide uptake in PRRT in meningiomas.[23] This information taken together with the physical properties of ^{177}Lu or ^{90}Y with a very limited maximal tissue penetration of the emitted β particles of 2 mm (maximum energy (Emax) 0.5 MeV) and 12 mm (Emax 2.3 MeV), respectively, allows for radiation dose estimation and consequently high tumor radiation doses, while minimizing the total radiation dose to normal brain parenchyma. As faster growing meningiomas have higher SUVmax, they will potentially also have higher radiation doses in PRRT. Accordingly, this treatment option might be particularly target-oriented. Furthermore, transosseous meningiomas elicited considerable high DOTATATE-binding; therefore, PRRT appears especially suited to complement surgery or external radiation therapy for skull base and spheno-orbito-maxillar meningiomas.

Finally, PET generates functional and morphological information that enhances treatment planning and dose calculation for IMRT.[20] Notably, PET morphometry facilitates more accurate delineation of skull base meningiomas when compared to contrast-enhanced MRI alone.[18]

WHO grade III meningiomas showed no correlation between SUVmax and TGR. Furthermore, the monthly growth was remarkably high with relatively low SUVs. This observation implies advanced dedifferentiation of the meningioma cells and limits the accuracy of predicting the growth rate with Ga^{68}-DOTATATE PET. The clinical role of the other PET tracers like the widely used F18-fluorodeoxyglucose (FDG) in patients with dedifferentiated meningioma is still not clear. Arita and colleagues did not find any correlation between 18 F-FDG uptake and WHO grading or tumor-doubling time.[30] On the other hand, Lee et al. reported that FDG uptake was a significant prognostic factor regarding tumor recurrence.[31] Regarding 18F-Fluoro-tyrosine and C11-Methionine,

markers of L-amino acid transport and protein synthesis, only small numbers of dedifferentiated meningioma were assessed in recently published studies,[32,33] thus their value as biomarkers for tumor growth rate or prognosis has not yet been established. Importantly, WHO grade III meningiomas show morphological features on MRI which help to diagnose this entity and guide PET use.[10] In meningiomas with an unclear tumor-brain interface, irregular tumor margins, heterogeneous contrast enhancement and missing capsular enhancement the probability of high-grade histology was 98%.[34] However, the present study does not allow any conclusion on the effect of PRRT on grade III meningiomas, as dedifferentiated cells may react differently to this therapy.

The study design was retrospective and therefore, a selection bias cannot be ruled out. Another potential limitation is the relatively high percentage of patients with multiple meningiomas; at least one lesion from these patients was histologically evaluated, but not all lesions were subjected to histological assessment. Previous studies revealed that multiple meningiomas usually display a uniform histology and anaplastic meningiomas (WHO grade III) were rare among these.[9,35] Therefore, we analyzed meningiomas of WHO grade I and II together.

SUV, reflecting the SSTR2-density measured by ^{68}Ga-DOTATATE PET, is a reliable predictor of TGR in WHO grades I and II meningiomas. This finding underlines its clinical importance for surgical planning and radiation therapy, since meningiomas with high SUVmax are at risk for progression and require either local or systemic treatment. Our study suggests that patients with high SUVmax might benefit from PRRT treatment, not only regarding dosimetric considerations but also with respect to risk for

progression. This holds especially true for transosseous meningiomas eliciting very high SSTR2 density. However, further studies are indicated to evaluate the therapeutic effect of PRRT in different histologic types of meningiomas and according to their SSTR2 expression.

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Figure captions

Figure 1: Correlation between tumor growth rate and SUVmax. Meningiomas separated into three different clusters (intracranial growth, transosseous growth and anaplastic meningiomas).

Figure 2: Examples of intracranial, transosseous and anaplastic meningiomas. From left to right baseline MRI, follow-up MRI and 68Ga-DOTATATE PET.

Reviewer #1: The authors studied 68Ga-DOTATATE PET in meningioma, and demonstrated a reliable predictive value for tumor growth in WHO grades I and II, using volumetric MR progression.

The paper is highly original and interesting, opening exciting perspectives for peptide receptor radionuclide therapy.

We thank Reviewer #1 for this appraisal of our study!

Some points should be addressed to improve the manuscript:

1/ tumoral progression was evaluated using MR with 4 to 20 months of temporal difference. The authors have to clarify if patients had treatments during this period, and if it is the case how they manage this information in the statistical model

We included detailed statements of concomitant therapy during the MR follow up time in the method section and added statistical analysis in the result section.
We did not find significant differences in SUVmax and tumor growth rate between treated and non-treated meningiomas. Correlation coefficient was stable in the group of intracranial meningiomas (r=0.770 vs r=0.757 in the whole group); however like because of low patient numbers (n=4), not to a significant degree.
We also added concomitant therapy as independent variable to multivariate analysis, which did not change results.

2/ no significant correlation was found between DOTATE uptake and tumor growth for anaplastic meningioma. The authors should strengthen the discussion with the contribution of other tracers at this dedifferentiated stage (especially FDG)

We added a paragraph in the discussion summarizing recently published studies regarding FDG-PET and PET markers of L-amino acid transport and protein synthesis (18F-Fluoro-tyrosine and C11-Methionine), commonly used in brain imaging.

We thank Reviewer #1 for the encouraging comments.

Reviewer #2: This manuscript looks at DOTATATE imaging in determining tumor growth rate (TGR).

Introduction is well-written.

Materials and Methods appear valid. The authors correlate growth rate with DOTATATE uptake. They separate intracranial meningioma from transosseous growth and WHO Grade III meningiomas.

We appreciate these comments.

Results demonstrate correlation of uptake with growth rate in intracranial meningioma and especially transosseous growth. Uptake does not correlate with WHO Grade III meningiomas.

It is unclear to me that Table 1-3 contributes to the content of this manuscript as it is quite raw and dense.

We included these tables with clinical data as well as our measurements to ensure transparence and comprehension of our findings. If you consider this information as unnecessary, we certainly agree to remove these tables.

Discussion is brief. They speculate this can be used to determine when treatment should be offered.

Our statement in the discussion: *The predictive value of TGR with Ga68-DOTATATE PET may be especially informative in meningiomas adjacent to delicate structures such as cranial nerves or arteries. Specifically, TGR with Ga68-DOTATATE PET may help in planning the optimal time point for surgery and for follow-up imaging. This is especially valuable for newly diagnosed meningiomas in such critical locations.*

It would be helpful if the authors can give some guidelines how to interpret these values as to when to initiate treatment.

Further studies have to assess these potential changes in management by the treating physician or the advisory tumor board in order to establish corresponding recommendations. (We added this statement to the above-mentioned text in the discussion)

They also speculate DOTATATE as radionucleide therapy, which is very interesting.

Overall, the data is reasonably presented. Figure 1 should include r values.

We added r values to Figure 1.

There are some spelling errors, including "somatostatin" on page 8, second paragraph. Also, meningioma is spelled wrong in key for Table 1.

We corrected mentioned errors and went carefully through the manuscript to check for spelling and grammar.

The data is certainly very interesting. Its applicability might be limited however as this is not a ubiquitous radiotracer.

We thank Reviewer #2 for the helpful comments.

Table 1: Intracranial meningiomas

ID	Age	Sex	WHO grade	Lesion with histology	Time between MRI scans [months]	Initial volume [mm^3]	Growth rate [%]	SUVmax [g/ml]
1	42.0	male	I	x	16	5726	14.58	22
						3107	15.51	26.1
						460	8.92	8.6
						431	22.88	32
*2	29.6	female	I/II		10	2561	1.87	6.3
			I/II			2312	3.77	6.8
			II	x		1689	21.51	19.1
			I/II			952	13.79	10
			I/II			795	7.51	6
**3	44.3	female	I		11	759	10.47	10.9
						544	13.67	15.1
						483	11.09	11.7
4	68.2	male	I		11	4142	14.71	14.9
						435	13.58	11.1
				x		345	10.58	10.7
				x		251	4.26	6
5	49.7	female	I		8	1841	12.76	16
				x		1054	18.38	18.8
						748	26.05	20.2
						483	16.40	15.9
						460	29.76	24
6	45.2	female	I	x	5	8186	4.33	9.3
7	42.5	female	II	x	6	483	4.91	4.8
						408	18.81	14.3
8	73.4	female	II		12	259	6.05	3.3
						157	6.92	4.6
				x		146	6.20	5.6
						94	6.50	4.5
9	62.0	female	II		13	314	8.09	9.7
				x		167	4.53	6
10	37.2	male	II		20	1849	0.82	3
						1657	28.81	17.4
				x		598	1.24	3.2
						366	0.81	2.6
						362	1.16	3.5
11	28.4	female	II	x	13	226	2.96	3.8
				x		176	4.04	4.2
						75	4.48	5
12	7.0	male	II	x	10	925	2.12	4.7
13	63.1	female	II	x	7	1255	7.08	7.5
14	68.1	female	II	x	6	316	1.83	7.1
						774	18.18	12.9
15	52.2	female	II		12	10632	3.38	22
						1245	2.24	20.9
				x		322	2.57	8
16	75.1	male	II		10	2457	10.72	14
				x		1809	3.18	7.6
17	64.5	female	II	x	11	63	0.16	2.9
***18	68.7	male	II		5	264	23.96	18.9
						188	13.91	15.7

* Patient with ID #2 had meningiomas with WHO grade I and II in histology (intrancranial and transosseus); therefore, menigiomas without biopsy were not allocated to a specific WHO grade (as indicated by ‘I/II’)

** Patient with ID #3 had intracranial and transosseous meningiomas, the latter was operated and histology was obtained

*** Patient with ID #18 received total resection of another meningioma from which histology was obtained

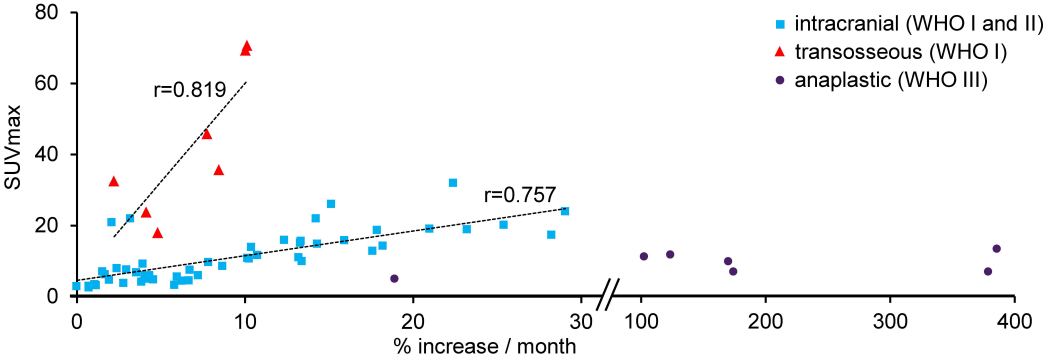
Table 2: Transosseous meningiomas

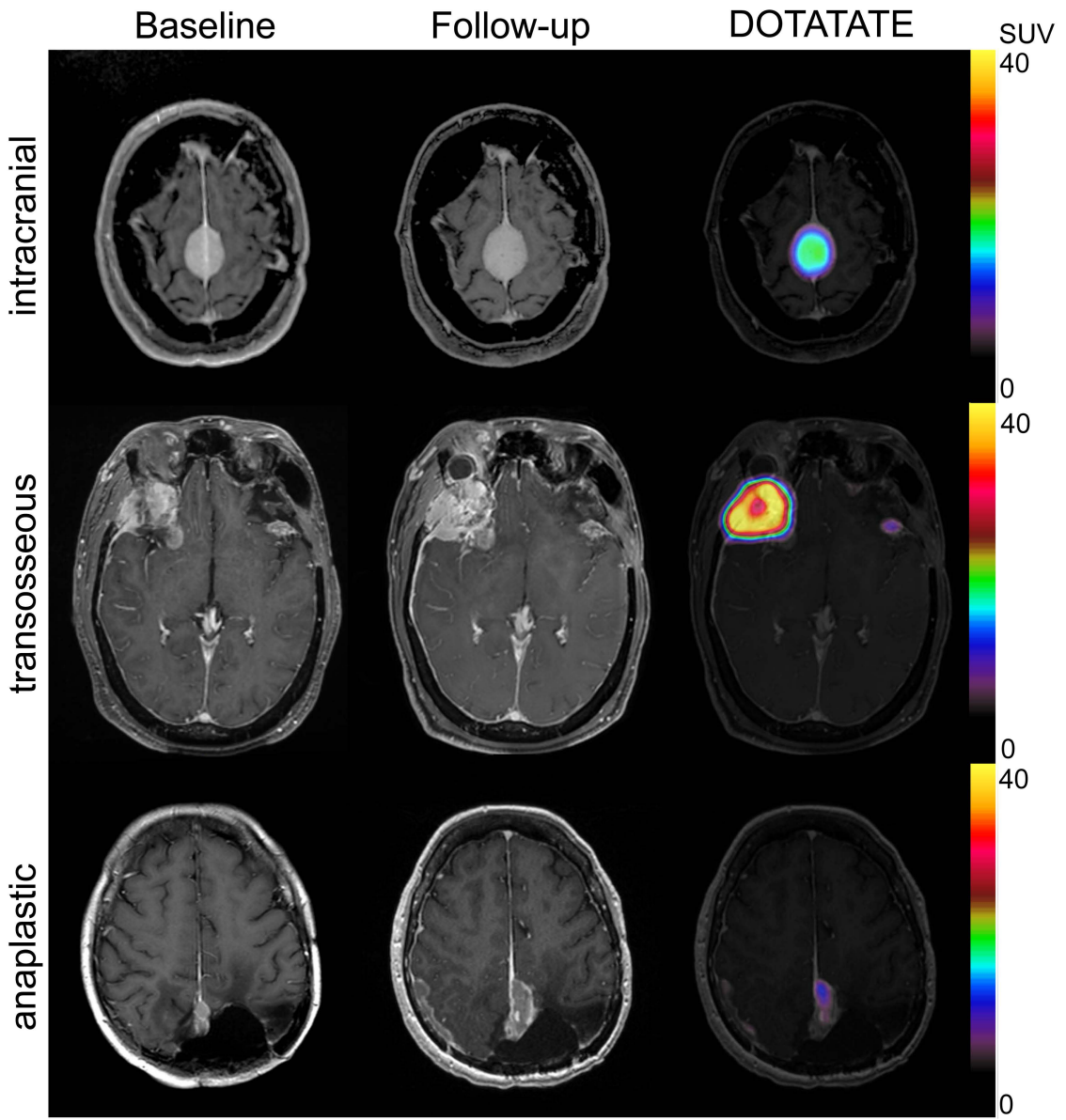
ID	Age	Sex	WHO grade	Lesion with histology	Time between MRI scans [months]	Initial volume [mm^3]	Growth rate [%]	SUVmax [g/ml]
*1	42.0	male	I	x	16	23995 1271 1391	10.32 7.98 4.31	69.3 45.8 23.8
*2	29.6	female	I	x	10	941	10.42	70.7
*3	44.3	female	I	x	11	1640	5.06	18
19	46.5	female	I	x	5	565	8.93	35.7
20	52.2	female	I	x	4	7362	2.67	32.5

*these patients elicited intracranial and transosseous meningiomas

Table 3: Anaplastic meningiomas

ID	Age	Sex	WHO grade	Lesion with histology	Time between MRI scans [months]	Initial volume [mm^3]	Growth rate [%]	SUVmax [g/ml]
21	39.0	female	III	x	7	31777	19.48	5
22	78.2	female	III	x	7	2921	104.42	10.7
23	61.8	female	III		7	1486	126.02	11.2
				x		205	173.29	9.4
						377	392.60	12.8
						78	177.53	6.6
						59	385.33	6.6


intracranial (WHO I and II)
transosseous (WHO I)
anaplastic (WHO III)
r=0.819
r=0.757
SUVmax
% increase / month
0
10
20
30
100
200
300
400
60
80


Baseline
Follow-up
DOTATATE
SUV
40
0
intracranial
transosseous
anaplastic